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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,817	05/13/2002	Jacques Edouard Germond	112843-039	9937

29174 7590 03/21/2003

BELL, BOYD & LLOYD, LLC
P. O. BOX 1135
CHICAGO, IL 60690-1165

EXAMINER
KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
1652	10

DATE MAILED: 03/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,817	GERMOND ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. The instant Office action is responsive to papers filed as of May 13, 2002. Claims 1-19 are pending in the instant Office action and will be examined herein.

Priority

2. The instant application is granted the benefit of priority for the European application 99112471 filed on June 30, 1999 and International Application No. PCT/EP00/05834 filed on June 23, 2000 as requested in the declaration. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Information Disclosure Statement

3. The information disclosure statement filed on December 20, 2001 (Paper No. 2) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Compliance with the Sequence Rules

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). A sequence listing in computer readable form and paper copy was filed on May 13, 2002 (Paper No. 5); said listing has been entered. However, this application fails to **fully** comply with the

requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) Figure 1 contains disclosure of DNA sequences without benefit of SEQ ID NOs.
b) Figure 2 contains disclosure of DNA sequences without benefit of SEQ ID NOs.
c) Figure 3 contains disclosure of DNA and protein sequences without benefit of SEQ ID NOs.

If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Objections to the Specification

5. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

> ---Expression Constructs Using the *Lactobacillus delbrueckii* subsp. *lactis* Lac Repressor Protein and Its Lac Repressor Binding Site, Microorganisms and Methods Thereof---

6. This application does not contain an abstract of the disclosure as required by 37 C.F.R. § 1.72(b). An abstract on a separate sheet is required.

7. The specification is objected to for being confusing with respect to the sequence listing. The sequence listing contains 22 sequences as filed on May 13, 2002 (Paper No. 5). Every SEQ ID NO is mentioned in the specification and/or the claims except SEQ ID NO: 22. It is unclear why said sequences are in the sequence listing if they are not described in the specification. All SEQ ID NOs in the sequence listing must be described in the specification. Appropriate correction is required.

8. The specification is objected to for the following inconsistencies:

a) On page 15, line 2, the pagination of the Gasson reference is incorrect.
b) On page 15, line 3, the J. Bacteriol. reference has no year of publication.
c) On page 19 (end of Example 3), the reference to Table 2 is confusing since all tables are denoted by Roman numerals.
d) On page 21, the Oskouian reference has an incorrect publication year.
e) On page 25 (bottom), the reference to Table V is confusing since no Table 5 has been filed.
f) On page 27 (bottom), the reference to Figure 12 is confusing since no Figure 12 has been filed.

Clarification and/or correction of all of the above points are required.

Claim Objections

9. Claims 1, 8, 13, and 17 are objected to for having improper punctuation and capitalization. The comma after "polypeptide of interest" must be a semi-colon. The "Y" in the last line must be lower case. Correction is required. Moreover, the Examiner notes that itemization (a, b, c...) in Claims 1, 8, 13, and 17 would be helpful in its clarity.

10. Claim 3 is objected to for improper word usage. The phrase "the reading frame of gene" must be written as ---the reading frame of <u>the</u> gene--- (emphasis added).

11. Claim 6 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In one aspect of Claim 6 (as interpreted due to a lack of clarity, see rejection below), the DNA claimed is SEQ ID NO:9 having a portion deleted, that portion being the 15 nucleotides of the CRE region identified as SEQ ID NO:8. The parent claim, Claim 1, requires the entire SEQ ID NO:9. Thus, Claim 6 is not contained within the scope of Claim 1 and does not properly further limit. Correction is required; the Examiner suggests a new, independent claim to correct the problem.

12. Claims 10 and 16 are objected to for having an improper Markush group. The phrase "selected from the group consisting of" is followed by only one option; this is *not* a group. This phrase must be deleted. Correction is required.

13. Claims 14 and 18 are objected to for improper word usage. The term "extra-chromosomal" must be written as the adverb ---extra-chromosomally---. Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-6 and 8-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The nature of the DNA sequence is unclear. The formula

presents no option for the sequence to be contained within, for example, a plasmid, as typically claimed using "comprising" language. The instant claims will be examined as if they are drawn to DNA sequences comprising the sequence represented by the general formula; clarification is required.

15. Claims 1-19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. References to the sequences described in the instant specification as being from *Lactobacillus delbrueckii* are unclear due to the different subspecies of the organism, wherein the sequences claimed are only found in one subspecies, the *lactis* subspecies (see Germond *et al.*, 2003). Each reference to the origin of the claimed sequences must refer to the proper organism, *Lactobacillus delbrueckii subsp. lactis* for clarity. Correction is required.

16. Claim 4 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The definition of the term "functional peptides" is unclear. All peptides have some function, but this term would not limit the parent claim is given this broad interpretation. Perhaps a particular function or set of functions is intended? Clarification is required.

17. Claim 6 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "catabolite responsive element" is unclear. In the specification, an example of a CRE is described on page 8, that is SEQ ID NO:8, which is embedded within SEQ

ID NO:9, the promoter region required to be a part of the DNA sequence. It is unclear if this region must be deleted from the claimed sequence or if any and all CRE's must be deleted. If the latter is true, the nature of a CRE, so that it can be discerned by one of ordinary skill in the art as a part of SEQ ID NO:9, is unclear. Clarification is required.

18. Claims 8-12 and 18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "recombinant" and "harboring" together imply that the microorganism claimed has been transformed with the noted DNA sequence; however, this is not an express limitation of the instant claims. Is transformation required? Clarification is required.

19. Claims 11 and 19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "bacteria's" does not have proper antecedent basis in the parent claims, Claim 8 or Claim 13, respectively. The Examiner suggests amending the term to ---microorganism's---. Correction is required.

20. Claim 12 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim is written as if the deposit numbers were microorganisms; however, by the descriptions of Figures 7-8, these are plasmids. The Examiner suggests substituting "which is" with ---wherein the DNA sequence is a plasmid --- for proper clarity. Correction is required.

21. Claims 13-17 and 19 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both methods, either directly or implied, focus on the expression of a polypeptide of interest. However, an option of the DNA expression construct is where n=0, i.e., no gene encoding a polypeptide of interest is present. It is confusing how these methods are productive without a gene encoding a polypeptide of interest being a part of the expression construct. Clarification is required.

22. Claims 13-17 and 19 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See M.P.E.P. § 2172.01. The instant claims are drawn to methods of producing a polypeptide by the use of a particular piece of DNA with the use of no particular method steps. As a whole, the instant claims are unclear. For Claim 13, the Examiner suggests steps such as a) transforming a host cell with the DNA and b) culturing said host cell under conditions favorable to the expression of the polypeptide of interest. For Claim 17, the Examiner suggests steps such as a) transforming a host cell with the DNA and b) using said host cell in the production of food products. Moreover, the Examiner notes that the specification describes the requirement of lactose for expression using the noted DNA constructs; said lactose binds the repressor protein inhibiting the binding of the repressor to the promoter region so that protein expression can take place. Thus, if claiming the expression of the polypeptide of interest, addition of lactose is also an essential method step that must be claimed. Correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claim 7 is rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 7 is drawn to DNA sequence that, optionally, is claimed solely by function ("or a functional variant") and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, genes encoding a lac repressor protein are described as any DNA sequence encoding SEQ ID NO:2. These genes are only described according to the functional characteristics of the enzyme they encode; no structural relationship is described or used in the claims. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure. Is there any required relatedness to a DNA sequence encoding SEQ ID NO:2? It is not required by the claim. Therefore, claims drawn to DNA containing the genus of said genes are also not adequately described. The Examiner suggests adding a structural limitation to the claimed "functional variant" or deleting the term.

24. Claim 12 is rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To produce the microorganism of Claim 12, one of skill in the art is required to use plasmids pLL112, pLL115, and pLL116. The instant specification contains no deposit information of these plasmids. To enable the instant claims by enabling the deposit of CNCM I-2089, I-2090, and I-2091, the following items are required: (1) the accession number assigned by the depository, (2) the date of deposit, (3) a brief description of the deposit, (4) the name and full address of the depository (37 C.F.R. § 1.801 - 1.809), and (5) the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative. Alternatively, Applicants can rebut

the instant rejection by a showing that the production of the instant plasmids is clearly described in the instant specification using only publicly available materials.

25. Claim 6 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for DNA sequences comprising SEQ ID NO:9 in the absence of the portion that is SEQ ID NO:8 (a catabolite responsive element or CRE), does not reasonably provide enablement for DNA sequences comprising SEQ ID NO:9 in the absence of some other portion of some other CRE sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To identify other CRE's in SEQ ID NO:9, considering a myriad of different catabolites, would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification presents no guidance or working examples for the identification of other CRE sequences within SEQ ID NO. No guidance of catabolites is presented as well. Numerous catabolites and portions of the sequence must be assayed to determine other CRE sequences. Such a discovery is wholly unpredictable in light of the information described in the instant specification in combination with the art. For these reasons, Claim 6 is not enabled to the full extent of its scope.

26. Claim 7 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for DNA sequences encoding SEQ ID NO:2, does not reasonably provide enablement for DNA sequences encoding functional variants of SEQ ID NO:2, the function being to bind SEQ ID NO:9. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To identify functional variants of DNA encoding SEQ ID NO:2 would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized above.

The instant specification presents no guidance or working examples for the identification of novel proteins that bind SEQ ID NO:9. The nature of the invention, considering the three-dimensional structures of proteins, is such that any structure, even those wholly unrelated to SEQ ID NO:2, may bind SEQ ID NO:9. No description of the functionally required elements of SEQ

ID NO:2 is found in the specification to aide the experimentation of one of skill in the art in identifying new, functionally similar proteins. Moreover, it is wholly unpredictable is such sequences exist naturally or if they can be engineered recombinantly. For these reasons, Claim 7 is not enabled to the full extent of its scope.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

27. Claims 1-6 are rejected under 35 U.S.C. § 101, utility, because the claimed invention is directed to non-statutory subject matter. Claim 1, as written, does not sufficiently distinguish over DNA as it naturally exists because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. Particularly, the Examiner notes that when n=0, as allowed by the limitation "$n \geq 0$", no heterologous gene is required in the DNA construct and the p/o region that is SEQ ID NO:9 is naturally located upstream of the R_y region that encodes SEQ ID NO:2. Thus, in the absence of a heterologous gene of interest (A_n), the claimed DNA sequence exists in nature. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" as taught by the specification. Alternatively, the limitation of n could be amended to $n \geq 1$. See M.P.E.P. § 2105.

The Examiner notes that Claims 8-12 and 18 are excluded from the instant rejection by virtue of the term "recombinant" in the claims which implies the hand of man. Additionally, the methods, Claims 13-17, are excluded from the instant rejection because neither a polypeptide nor a food product are produced when n=0.

28. Claim 7 is rejected under 35 U.S.C. § 101, utility, because the claimed invention is directed to non-statutory subject matter. Claim 7, as written, does not sufficiently distinguish over DNA as it naturally exists because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" as taught by the specification. See M.P.E.P. § 2105.

Additional References

29. The following references are cited to complete the record; they are post-filing date art:

a) **Germond *et al.*** Evolution of the Bacterial species Lactobacillus delbrueckii: A partial Genomic Study with Reflections on Prokaryotic Species Concept. Mol. Biol. Evol. (2003) 20(1):93-104. Noted above in a rejection under 35 U.S.C. § 112, second paragraph.
b) **Lapierre *et al.*** Regulation and Adaptive Evolution of Lactose Operon Expression in Lactobacillus delbrueckii. J. Bacteriol. (2002) 184(4):928-935.

Allowable Subject Matter

30. SEQ ID NO:9 is free of the prior art; said sequence is from the lac operon of *Lactobacillus delbrueckii* subsp. *lactis*. The promoter region, SEQ ID NO:9, is different among other subspecies of *L. delbrueckii* as evidenced in the specification and the post-filing date (Germond *et al*, 2003). Although portions of SEQ ID NO:9 may be taught in the prior art in the form of IS elements from the subspecies *bulgaricus*, the full-length of SEQ ID NO:9 is not taught in the prior art and is required in all the pending claims except Claim 7. Moreover, no evidence that the IS elements previously found were located as a part of SEQ ID NO:9 in subspecies *lactis*, with or without sequence information, as presented in the instant specification.

Any DNA sequence encoding SEQ ID NO:2 is also free of the prior art; SEQ ID NO:2 is a lac repressor protein from *Lactobacillus delbrueckii* subsp. *lactis* that is a part of the lac operon.

Leong-Morgenthaler *et al.* (see IDS) teach a lac operon from *L. delbrueckii* subsp. *bulgaricus* wherein the DNA sequence upstream of the permease gene, that is the same location as SEQ ID NO:9 taught in the instant specification, is similar (~75% identity) to SEQ ID NO:9; however, neither SEQ ID NO:9 nor isolated portions of the lac operon from subspecies *lactis* are taught in the prior art. Moreover, no homolog to lacR, the repressor found in the operon of *L. delbrueckii* subsp. *lactis* described in the instant specification, is taught by Leong-Morgenthaler *et al.* In fact, Germond *et al.* (2003) particularly note that ONLY the subspecies *lactis* contains the lacR repressor protein in the lac operon of all the *L. delbrueckii* subspecies.

Claim Language Suggestion

31. The following are suggested claim language amendments incorporating various corrections for the above cited rejections:

a) ---Claim 1. An isolated DNA expression construct comprising a DNA sequence represented by a general formula selected from the group consisting of:

p/o - $(A)_n$ - R_y, and

p/o – R_y – $(A)_n$

wherein

i) p/o is a *Lactobacillus delbrueckii* subsp. *lactis* promoter that is SEQ ID NO:9,

ii) A is a heterologous gene encoding a polypeptide of interest, and

iii) R is a gene encoding the *Lactobacillus delbrueckii* subsp. *lactis* lac repressor protein that is SEQ ID NO:2;

and wherein n denotes an integer ≥ 1 and y denotes 0 or 1.---

b) Dependent Claims 2-5 should be amended to ---The DNA expression construct according to claim 1...--- (emphasis added).

c) ---Claim 7. An isolated DNA sequence encoding the lac repressor protein of *Lactobacillus delbrueckii* subsp. *lactis* as identified by SEQ ID NO:2.---

d) ---Claim 8. A recombinant microorganism transformed with a DNA expression construct according to Claim 1---.

e) Amendments to claims not noted above should be considered in light of the above rejections.

Conclusion

32. Claims 1-19 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
March 20, 2003